REMARKS

Claims 26 and 28-49 are pending. Claims 26 and 28-49 are rejected. The Specification is amended herein with support from the Application Data Sheet. Claims 26 and 45 are amended herein without acquiescence and without prejudice. The amendment to claim 26 finds support in the Specification at least in Example 1, Page 77, Lines 21-24. The amendment for claim 45 finds support at least in original claims 19 and 20. Applicants assert that no new matter has been added.

I. Specification objection

The Examiner objects to the Specification because of an informality relating to cross reference to PCT/GB03/01213, U.S. Application No. 10/102,622, and U.S. Application No. 60/366,058. The Specification is amended herein to reference the above-mentioned applications. Applicants assert that no new matter has been added.

The Applicants respectfully request withdrawal of the objection.

The Applicants also note on Page 2 of the Action that the Examiner provides guidelines for the layout of the Specification. Because the guidelines were suggested only, Applicants will take no action at this time.

II. Double patenting rejections – U.S. Application 10/380,981 in view of Kotsopoulou

Claims 26, 28-34, 37-39, and 40-42 are provisionally rejected by the Examiner on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, and 9-15 of copending Application No. 10/380,981, in view of Kotsopoulou *et al.,* J Virol, 2000, 74:4839-4952 ("Kotsopoulou").

Application No. 10/380,981 has been abandoned in favor of a continuation application, U.S. Application No. 11/764,814. However, the court of Claims and Patent Appeals (now the Court of Appeals for the Federal Circuit) has stated: "Once the provisional rejection has been made, there is nothing the examiner and the applicant must do until the other application issues." *In re Mott,* 190 U.S.P.Q. 536, 541 (C.C.P.A. 1976). MPEP § 804 allows for the prosecution to continue while a provisional double-patenting rejection is

pending and even instructs the Office to continue to make such a provisional rejection until one of the applications issues as a patent.

Thus, Applicants request that the rejection be held in abeyance until the conflicting claims are in fact patented.

III. Double patenting rejections – US Application 10/508,143 in view of Kotsopoulou and Woodberry

Claims 26, and 28-43 are provisionally rejected by the Examiner on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 7-11 of copending Application No. 10/508,143, in view of Kotsopoulou and Woodberry *et al.,* J Virol, 1999, 73:5320-5325 ("Woodberry").

As stated above, the court of Claims and Patent Appeals (now the Court of Appeals for the Federal Circuit) has stated: "Once the provisional rejection has been made, there is nothing the examiner and the applicant must do until the other application issues." *In re Mott,* 190 U.S.P.Q. 536, 541 (C.C.P.A. 1976). MPEP § 804 allows for the prosecution to continue while a provisional double-patenting rejection is pending and even instructs the Office to continue to make such a provisional rejection until one of the applications issues as a patent.

Applicants request that the rejection be held in abeyance until the conflicting claims are in fact patented.

IV. 35 U.S.C. § 112, 2nd paragraph rejection

Claims 26 and 45 are rejected under 35 U.S.C. § 112, 2nd paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 45 is amended herein without acquiescence and without prejudice. Current claim 45 now reads on exon 1 of the HCMV IE gene, and is dependent on claim 44. The Examiner states in the Action that "amending claim 45 to recite the first exon of the IE-1 and to depend from claim 44 would obviate this rejection." Thus, by the Examiner's own statement, the metes and bounds of claim 45 as amended can be determined and the claim is definite.

Applicants also note that claim 26 is listed as being rejected on Page 9 in the 35 U.S.C. § 112, 2nd paragraph, rejection section header 8. Applicants note that claim 26 lacks the element of a heterologous promoter comprising exon 1 and respectfully request clarification of this issue.

Applicants respectfully request withdrawal of the rejections.

V. 35 U.S.C. § 103(a) – Woodberry in view of Peter, Goulder, and Miller

Claims 26, 28, 29, 36-38, 42, and 47-49 are rejected by the Examiner under 35 U.S.C. § 103(a) as being allegedly unpatentable over Woodberry, in view of Peter *et al.,* Vaccine, 2001, 19:4121-4129, Abstract ("Peter"), Goulder *et al.* Immunol. Lett., 2001, 79:109-116, Abstract ("Goulder"), and Miller WO 93/20847 ("Miller"). Applicants traverse.

The Examiner states on Page 10 that "Woodberry et al. taken with Peter et al. and Goulder et al. do not teach using imiquimod as adjuvant," and further states on Page 11 that "although Miller et al. teach administering imiquimod after the vaccine administration (i.e., 48 hours), they do not specifically teach 12 to 36 hours." The Examiner provides no further reference to teach the 12 to 36 hour administration of imiquimod as is recited in the instant invention. The Examiner's rejection is then based off the assumption that it would have been obvious to one of ordinary skill in the art to vary the parameters in the method with the purpose of optimizing the results and that such conditions can be identified by routine experimentation. However, this is not the case, and the Applicants request that the Examiner find support for the assumption with adequate evidence (MPEP § 2144.03 C).

The requirement for the imidazo compound to be administered 12 to 36 hours after the vaccine is an aspect of the instant invention. This is illustrated by the Examples in the application. The Examiner made the rejection "[a]bsent evidence of unexpected results" (the Action, page 11), but the Examples provide such evidence. Applicants refer the Examiner to Examples 1, 2 and 7 within the specification, wherein the exemplary results show that administration of the imidazo compound one day after immunization with the vaccine gave a significant immune response; see especially Table 1 on Page 83 and Figure 16.

Although Applicants assert that the use of the 12 to 36 hour time window specified in the claims was not obvious from the combined teachings of Miller, Woodberry, Peter and

Goulder, solely to further prosecution of this case, Applicants clarify the claims by amending claim 26 to recite that the compound is administered only 12 to 36 hours after the nucleic acid vaccine is administered. None of the references disclose or suggest that administration regimen for that time window. The fact that the present Examples demonstrate that such an advantage exists was entirely unpredictable from the references. Further, the amendment to claim 26 clarifies that the imidizo compound is not given simultaneously with the vaccine, but is only administered between the window of 12-36 hours after the initial vaccine was given.

The only reference that contains any teaching that is even remotely relevant to the time window required by the present claims is Miller. As noted by the Examiner, Miller teaches about the use of imidazoquinoline amines as adjuvants. However, Miller merely contains a generic disclosure that the imidazo compound should be administered simultaneously or after (e.g. 48 hours after) immunization with the vaccine (see especially page 15, lines 17-30 and page 28, lines 1-21). Miller does not disclose the sole and specific time window of 12 to 36 hours required by the present claims or suggest that there would be any advantage in using this time window in addition to Applicants' claimed administration regimen.

The administration regimen used by Miller teaches away from the instant invention. Miller teaches using 5 mg/kg/day *for five consecutive days* starting either concurrently with or 48 hours after vaccination (Miller, Page 28, Lines 1-12). Here we see that Miller teaches administration over the course of five days for therapeutic effectiveness of the adjuvant. The claims herein recite the use of only the specific 12 and 36 hours after vaccination. Further, Example 1 and Figure 1 of the Specification show that administration of the adjuvant only in the 12 to 36 hour time window is superior to administration daily for three days on days 0, 1 and 2, in one embodiment of the invention. This result is unexpected given the disclosure of Miller.

Neither has the Examiner establish a *prima facia* case of obviousness nor identified the reason that would have prompted one of skill in the art to combine the references given the instant invention. The court maintains that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements." *KSR International v. Teleflex Inc.*, Supreme Court No. 04-1350, April 30, 2007. As Miller teaches

away from the invention by teaching administration over the course of five consecutive days, as opposed to administration only in a certain time window, one of skill in the art would not use the combination of Miller and Woodberry to develop the instant invention.

The Examiner made subsidiary rejections under 35 USC 103 that focused on dependent claims. Those rejections are unfounded for the reasons given above; all the dependent claims incorporate the subject matter of claim 26 and therefore set forth unobvious subject matter for at least the reasons given above.

Applicants respectfully request withdrawal of the rejections.

VI. 35 U.S.C. § 103(a) – Woodberry, Peter, Goulder, and Miller, further in view of Zhang and Kotsopoulou

Claims 26, 28, 29, 36-43, and 46-49 are rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Woodberry taken with Peter, Goulder, and Miller, in further view of Zhang *et al.,* Immunol. Lett., 2001, 79:93-96 (Zhang") and Kotsopoulou. Applicants traverse.

The Examiner uses the additions of Zhang to teach use of p24 and Kotsopoulou to teach the use of codon optimized Gag and Pol. The Applicants note that claims 26, 28, 29, 36, 37, 42, 46, and 49 lack either element mentioned by the Examiner and provided in the additional Zhang and Kotsopoulou references and are thus, improperly included in this section. Nevertheless, to establish *prima facia* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). As previously argued in section V, the references cited, now including Zheng and Kotsopoulou, do not teach or suggest each element of amended independent claim 26. Specifically, none of the cited references teach the 12-36 hour time frame and administration regimen for administration of the adjuvant. As all other rejected claims depend from independent claim 26, each dependent claim contains all the limitations of the independent claim. Thus, a *prima facie* case of obviousness has not been established for any of the rejected claims.

Applicants respectfully request withdrawal of the rejections.

VII. 35 U.S.C. § 103(a) – Woodberry, Peter, Goulder, and Miller, further in view of Fynan and Spruance

Claims 26, 28-38, 42, and 47-49 are rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Woodberry taken with Peter, Goulder, and Miller, in further view of Fynan *et al.,* Proc Natl Acad Sci, 1993, 90:11378-11482 ("Fynan") and Spruance *et al.* The Journal of Infectious Disease, 2001, 184:196-200 ("Spruance"). Applicants traverse.

The Examiner uses the additions of Fynan to teach the use of a gene gun and Spruance to teach the administration of a gel. The Applicants note that claims 26, 28, 29, 36-38, 42, and 47-49 lack either additional element mentioned by the Examiner and provided in the additional Fynan and Spruance references and are thus, improperly included in this section. Nevertheless, to establish *prima facia* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). As previously argued in section V, the references cited, now including Fynan and Spruance, do not teach or suggest each element of independent claim 26. Specifically, none of the cited references teach or suggest only administration in the 12-36 hour timeframe for administration of the adjuvant. As all other rejected claims depend from independent claim 26, each dependent claim contains all the limitations of the independent claim. Thus, a *prima facie* case of obviousness has not been established for any of the rejected claims.

Applicants respectfully request withdrawal of the rejections.

VIII. 35 U.S.C. § 103(a) – Woodberry, Peter, Goulder, and Miller, further in view of Mikkelsen

Claims 26, 28, 29, 36-38, 42, 44, 45 and 47-49 are rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Woodberry taken with Peter, Goulder, and Miller, in further view of Mikkelsen *et al.,* Transgenic Research, 1992, 1:164-169. Applicants traverse.

The Examiner uses the additions of Mikkelsen to teach the use of HCMV IE-1 to drive gene expression. The Applicants note that claims 26, 28, 29, 36-38, 42, and 47-49 lack the additional element mentioned by the Examiner and provided in the additional Mikkelsen

reference and are thus, improperly included in this section. Nevertheless, to establish *prima facia* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). As previously argued in section V, the references cited, now including Mikkelsen, do not teach or suggest each element of independent claim 26. Specifically, none of the cited references teach only administration within the 12-36 hour timeframe for administration of the adjuvant. As all other rejected claims depend from independent claim 26, each dependent claim contains all the limitations of the independent claim. Thus, a *prima facie* case of obviousness has not been established for any of the rejected claims.

Applicants respectfully request withdrawal of the rejections.

CONCLUSION

Applicant believes no fee is due with this response other than the fee for the Petition for Extension of Time of Three Months. However, if another fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P03173US0 from which the undersigned is authorized to draw.

Dated: May 15, 2008

Respectfully submitted,

By /Melissa L. Sistrunk/

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